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Marc De Block

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04/28/2009

HUNTON & WILLIAMS LLP
INTELLECTUAL PROPERTY DEPARTMENT
1900 K STREET, N.W.
SUITE 1200
WASHINGTON, DC 20006-1109

EXAMINER

KUMAR, VINOD

ART UNIT

PAPER NUMBER

1638

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

| | | | |
|------------------------------|--------------------------------------|---------------------------------------|--|
| Office Action Summary | Application No. 10/552,552 | Applicant(s) DE BLOCK, MARC | |
| | Examiner VINOD KUMAR | Art Unit 1638 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 November 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 9-16 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 9-16 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 07 October 2005 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114 was filed in this application after appeal to the Board of Patent Appeals and Interferences, but prior to a decision on the appeal. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on 11/20/08 has been entered. Applicant's response filed 9/17/2008 (after Final) is also entered.

Status of Objections and Rejections

2. Claims 1-8 and 17-21 are previously cancelled.
3. Claims 9-16 are pending.
4. Claims 9-16 are examined on merits in the present Office action.
5. The objection to claim 14 has been withdrawn in light of claim amendment filed in the paper of 9/17/08.
6. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.
7. Rejection of claims 9-16 under 35 U.S.C. 112, 2nd paragraph has been withdrawn in light of claim amendment filed in the paper of 9/17/08.
8. Rejection of claims 9-16 under 35 U.S.C. 102(a) has been withdrawn in light of persuasive arguments filed in the paper of 9/17/08.

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Claim Objections

9. Claims 9 and 16 are objected to because of the following informalities:

Claim 9 is objected for not reciting expression of the DNA molecule in part (III) of claim. It is suggested to change “wherein introduction of the DNA molecule into a plant results in a plant tolerant to high light stress” to --wherein introduction and expression of the DNA molecule into a plant results in the plant tolerant to high light stress as compared to a plant that does not comprise said DNA molecule--.

Claim 16 is objected for lacking space between “(iii)” and “a” in line 18.

In claim 16, it is suggested to insert --as compared to a plant that does not comprise said chimeric gene-- at the end of claim.

Appropriate corrections are required.

Claim Rejections - 35 USC § 112

10. Claims 9-16 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a DNA molecule comprising a plant expressible promoter operably linked to an 163 bp of ParG coding sequence of SEQ ID NO: 3 (positions 973 to 1135) in sense and antisense orientation separated by an intron, and further operably linked to 3' transcription termination signals, to produce an inhibitory double-stranded RNA molecule when expressed in transgenic *Arabidopsis*, *Brassica* or tobacco plant, and wherein said transgenic plant exhibits high light stress tolerance, or a method of producing said transgenic plant using said DNA molecule, does not reasonably provide enablement for a DNA molecule comprising at least 40, 50 or 100

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nucleotides in sense and antisense orientation from any region of a nucleotide sequence encoding the protein of SEQ ID NO: 1. The claims contain subject matter which was not described in the specification in such a way as to enable any person skilled in the art to which it pertains, with which it is most nearly connected, to make and use the invention commensurate in scope with these claims for the reasons of record as stated in the Office action mailed 3/17/08. Applicant traverses the rejection in the paper filed 9/17/08.

Applicant argues that claims 9 and 16 have been amended to refer to a sense and antisense nucleotide sequence of at least 40 consecutive nucleotides. Applicant further cites Thomas et al. to argue that fragments of at least 23 nucleotides long could induce silencing of the target (response, page 6, lines 14-25).

Applicant's arguments are carefully considered but are deemed to be unpersuasive.

It is noted that size of a DNA fragment required to silence endogenous plant genes is highly unpredictable. Applicant's attention is drawn to table 3 (pg 422) of Thomas et al. (cited by Applicant), wherein it is quite evident that even a fragment of 52 nucleotides (sense or antisense) was unable to down regulate the expression of endogenous plant phytoene desaturase. It is also important to note that Thomas et al. do not teach down regulation of endogenous plant gene using a double stranded inhibitory RNA molecule as instantly claimed.

It is maintained that using DNA sequences to reduce expression of the endogenous corresponding gene through the mechanism of antisense/sense or dsRNAi

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based suppression methods is highly unpredictable. See for example, Arziman et al. (Nucleic Acids Research, 33:582-588, 2005) who teach that although a dsRNA should be designed to match to one specific gene, off-target effects can occur if SiRNAs have sequence homology to genes that are not supposed to be targeted. The knock-down of target might differ depending on the efficiency of SiRNA derived from long dsRNA. It is further maintained that the stability of a double-stranded RNA would also depend upon a number of factors, such as sequence composition (e.g., GC content), thermodynamic stability and sequence length etc.

While the specification provides guidance on using 163 bp region (positions 973 to 1135) of SEQ ID NO: 3 in obtaining ParG gene suppression effect in transgenic *Arabidopsis* and tobacco plants, it does not provide guidance whether sequences of at least 40, 50 or 100 bp in size and derived from any region of a nucleotide sequence encoding SEQ ID NO: 1 would produce ParG gene suppression effect when expressed in said plant species.

It is also noted that amended claim 9 reads on reducing the expression of a ParG gene in any plant using instantly claimed DNA molecule. The specification fails to provide guidance that instantly claimed inhibitory DNA molecule would produce gene silencing of an endogenous ParG gene in any plant species as encompassed by the breadth of claim 9.

In the absence of guidance, it is maintained that undue experimentation would have been required by a skilled artisan to determine how to use 40, 50 or 100 consecutive bp of a nucleotide sequence encoding SEQ ID NO: 1, in a method of

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obtaining high light stress tolerance transgenic plant through the gene suppression of endogenous ParG gene expression in said plant. See Genentech, Inc. v. Novo Nordisk, A/S, USPQ2d 1001, 1005 (Fed. Cir. 1997), which teaches that “the specification, not the knowledge of one skilled in the art” must supply the enabling aspects of the invention.

Accordingly, the rejection is maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

11. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 9-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chang et al. (WIPO, WO 03/000898, Published January 3, 2003, Applicant's IDS), and

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further in view of Wesley et al. (The Plant Journal, 27:581-590, 2001) and Panda et al. (Developmental Cell, 3:51-61, July 2002; Applicant's IDS).

Chang et al. teach a transgenic plant and a method of making a transgenic plant comprising transformation of said plant with a DNA expression cassette comprising a plant-expressible promoter operably linked to a ParG (poly(ADP-ribose) glycohydrolase) nucleotide sequence as defined in SEQ ID NO: 550 which is identical in sequence to instant SEQ ID NO: 3, and wherein said nucleotide sequence is in antisense orientation relative to the promoter, and transcribes to yield a ParG molecule which inhibits the expression of endogenous ParG expression of the transformed plant. The reference also teaches down-regulation of endogenous ParG gene expression in a plant comprising transformation of a DNA construct comprising sense and/or antisense sequences of SEQ ID NO: 550 to down-regulate or inhibit endogenous ParG gene expression in said plant. The reference discloses seeds of the transformed plant and a method of transferring said DNA expression cassette to a non-transgenic plant through crossing between said transgenic plant and the plant lacking said DNA expression cassette. The reference also teaches transgenic *Arabidopsis* or *Brassica* plants comprising said DNA expression cassette. The reference also teaches that said expression cassette further comprises a 3' end region involved in transcription termination and polyadenylation. The reference also teaches that said transgenic plants are produced by transforming plant (*Arabidopsis* or *Brassica* or tobacco) cells with said expression cassette (designed to produce inhibitory RNA molecule) and subsequent regeneration and identification of the transgenic plant with the expected phenotype.

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See in particular, SEQ ID NO: 550; claims 27-57, 57-58, 63-67; page 34, lines 23-29; pages 53, 98-99, 100-108.

Chang et al. do not teach using RNAi (double stranded inhibitory RNA) based method of down-regulating endogenous plant gene expression.

Wesley et al. teach hpRNA (hairpin RNA) (same as RNAi; double stranded inhibitory RNA) based method of gene silencing in plants. The reference also teaches that double-stranded inhibitory RNA is a highly efficient method of silencing endogenous plant genes when compared to sense, antisense or co-suppression based methods of silencing or suppressing plant gene expression. The reference further teaches that about 90-100% independent transgenic plant exhibit gene silencing using this method. The reference also teaches a method of making DNA constructs which produce double stranded inhibitory RNA upon expression in a plant. See in particular, page 581, abstract; page 582, figure 1; page 585, figure 3; page 586, figure 4; page 587, table 1, figure 5; page 588, figure 6; pages 588-589, materials and methods.

Panda et al. teach the function of ParG (poly(ADP-ribose) glycohydrolase) by isolating *Arabidopsis* mutants disrupted in ParG expression. The mutants were tolerant to high light stress. The reference also teaches restoring wild-type function in said mutants by complementing with a wild-type ParG using *Agrobacterium* mediated plant transformation method. See in particular, 51, abstract; pages 53-58, figures 1-6; pages 59-60, materials and methods.

At the time the invention was made, it would have been *prima facie* obvious, and within the scope of an ordinary skill in the art to modify Chang et al. sense, antisense or

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cosuppression constructs by designing ParG RNAi (double stranded inhibitory RNA) construct using any method of designing RNAi construct including the one taught by Wesley et al. to suppress the endogenous ParG gene expression with a reasonable expectation of success.

Given that Panda et al. clearly teach that disrupting ParG gene expression leads to increased tolerance to high light stress, it would have been obvious and within the scope of an ordinary skill in the art to inhibit endogenous plant ParG gene expression by transforming a plant with an RNAi inhibitory construct as discussed above to produce high light stress tolerant transgenic plants with a reasonable expectation of success.

Obviously seeds would have also been produced for the purpose of propagation.

Thus, the claimed invention as a whole is prima facie obvious over the combined teachings of the prior art.

Conclusions

13. Claims 9-16 remain rejected.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vinod Kumar whose telephone number is (571) 272-4445. The examiner can normally be reached on 8.30 a.m. to 5.00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg can be reached on (571)272-0975. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Vinod Kumar/
Examiner, Art Unit 1638